VISUAL EVOKED RESPONSES AND EEGS FOR DIVERS BREATHING HYPERBARIC AIR: AN ASSESSMENT OF INDIVIDUAL DIFFERENCES

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SUMMARY PAGE

THE PROBLEM

To find and assess quantitatively electrophysiological correlates of nitrogen narcosis in divers.

FINDINGS

Marked decrements in visual evoked responses were found in most divers under conditions conducive to nitrogen narcosis. Results of this study show the average sizes of the decrements and their probability of occurrence in a large group of subjects.

APPLICATION

Since nitrogen narcosis is a major problem deterring air dives to 200 ft or more, these results should help in understanding the narcosis and in assessing the roles of experience and of individual differences in susceptibility in its occurrence.

ADMINISTRATIVE INFORMATION

This investigation was conducted as part of Bureau of Medicine and Surgery Research Unit MF51.524.004-9015. The present report is Number 12 on this work unit. It was submitted for review on 7 May 1975, approved for publication on 3 June 1975, and designated as NavSubMedRschLab Report No. 809.

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ABSTRACT

In order to assess individual differences in susceptibility to nitrogen narcosis, a group of 16 men made repeated air dives to approximately 200 ft in a pressure chamber. The visual evoked response of the men at depth revealed several decrements: in the response to a slow rate of stimulation, there was a highly significant reduction in a component around 160 msec; in the response to a rapid rate of stimulation, marked losses in amplitude and increases in variability were found. The latter changes were related to diving experience while the former were not. No significant changes were found in alpha or theta activity in the EEG.

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VISUAL EVOKED RESPONSES AND EEGS FOR DIVERS BREATHING HYPERBARIC AIR: AN ASSESSMENT OF INDIVIDUAL DIFFERENCES

INTRODUCTION

The evoked cortical potential or the response evoked by sensory stimulation has been used by numerous investigators to assess brain functioning of divers under a wide variety of conditions. Auditory,[1-3] visual,[4-9] and somatosensory[10-12] evoked responses have all been used and there is general agreement that marked decrements are found when divers breathe air at depth. The decrements are generally attributed to narcosis since the substitution of helium-oxygen as a breathing mixture eliminates both the evoked response decrements and the subjective and behavioral indications of narcosis.[1,2,4,5,10]

Despite the general unanimity of these reports, several questions remain unanswered. First is the theoretical one of the underlying basis of the decrements. Many investigators have assumed that they reflect changes in cortical functioning; this is largely due simply to the fact that both narcosis and evoked responses involve the Central Nervous System (CNS). The data of Ackles and Fowler[13] and of Bennett[14] have shown this explanation to be too simple however. While it is true that all gases which yield subjective narcotic symptoms (i.e., nitrogen, argon, nitrous oxide[15]) also yield decrements in the evoked response, the size of the decrement is not predictable from the narcotic potency of the gas. A number of explanations of evoked response decrements might be postulated: for example, an asymptotic effect in the CNS which is reached at depths around 300 to 400 ft while breathing air; differential sensitivity to narcosis of various cortical sites subserving perception, memory, or subjective feelings, etc.; or more peripheral mechanisms changed somehow by the heavier and not the lighter gases. At present, however, there is limited data available to choose among the various speculations.

Second is the practical question of the consistency of visual evoked responses (VER) in decrements among individuals. While it is true that average data, for a group of subjects, reveal decrements in evoked responses at depth, it is also true that this is not true for every subject. Since the number of subjects employed in a given chamber dive is generally quite small, often only one or two, interpretation of the data becomes very difficult. For example, VERs and EEGs obtained during shallow habitat saturation dives (SHAD I and II) sometimes showed an effect for one subject and the opposite for the other.[7]

Finally, another practical question concerns individual differences in EEG response during hyperbaric exposure. Routine EEGs are generally monitored during any unusual exposure to pressure in order to assure the safety of the divers.[16-19] Adverse symptoms are generally not found, except in situations conducive to the high-pressure nervous syndrome.[20] However, when unusual effects do occur, they are often difficult to interpret because of a paucity of experimental data and the individual differences commonly found. Analysis of EEG data for a large number of subjects, under hyperbaric pressure, would aid immensely in this interpretation.

A series of dives, therefore, was designed to provide answers to these questions. Repeated bounce dives to about 7 ATA were made by a group of 16 men while breathing air; the men varied considerably in the amount of prior diving experience. A variety of measures, behavioral, neurophysiological, and biochemical, were made on all the divers. The degree of correlation among these various tests will be the basis of a future report; it should help answer many questions concerning the etiology of narcosis.

This paper reports on the electrophysiological measures, both VERs and EEGs, made on the 16 men. Since this is an exceptionally large group, for diving research, it provides data as to the size of individual differences and their practical evaluation.

PROCEDURE

VERs were recorded from bipolar electrodes with the active electrode at O_Z, over the primary visual cortex, the reference at C_Z, and a ground electrode on the ear. The signal was fed, through a short connection through the chamber wall, to a Grass pre-amplifier, a Computer of Average Transients, and a Tektronix oscilloscope, for on-line analysis and monitoring, and to a Hewlett-Packard tape recorder. One hundred, one-second intervals of EEG were averaged for each VER.

The stimulus for the VERs was a pattern of vertical stripes, formed of opaque and clear material, placed over the porthole; the pattern was backlighted by a Grass PS-2 photo-stimulator set at the arbitrary intensity of 16. At the diver's observing distance of 28 inches, the overall pattern subtended an angle of ten degrees and each individual stripe one degree of visual angle. Two different flash rates were employed to illuminate the striped pattern, one flash per second and 16 flashes per second.

For recording EEGs, the same electrodes and equipment were used, except that there was no visual stimulus and the signal was recorded on a portable polygraph and on magnetic tape for later analysis. This consisted of measurement of the amplitude of response at each frequency, in 1/4-Hertz steps, by a Federal Scientific Spectrum Analyzer and Averager.

For each recording session, the subject sat with his chin in a chinrest, looking at the porthole. The striped target was then illuminated at a rate of 16 flashes per second and a VER recorded. Following this, the subject was told to sit quietly with his eyes open while EEG was recorded for 90 seconds. The striped target was next illuminated at a rate of one per second; this was followed by 90 seconds of EEG with the eyes closed. The entire session took six to seven minutes, and was repeated prior to the dive, at the limit of the planned "depth" of the simulated dive, and, for some of the subjects, at decompression stops at 20 and 10 feet.

DIVING PROFILE

The data were collected in several phases, over a period of two years. During this time, several details of the experimental protocol were changed, due to diving regulations, scheduling problems, and as a result of the interpretation of the accumulating results. However, the major features of the diving procedures remained the same. They were bounce dives to about seven atmospheres; the breathing mixture was air; the compression rate, 60 ft per minute; and the bottom time, forty-five minutes. VERs and EEGs were recorded just prior to compression and five minutes after arrival at the bottom.

The protocol for the first eight men, who were run from Aug to Oct, 1972, included two dives each to two and to seven atmospheres (198 ft), in a counterbalanced order. Each man was scheduled for a dive once a week for the four-week period that it took to complete his schedule. The men were not told the depths to which they were subjected; this was to enable use of the 2 ATA data as a control for the 7 ATA. However, since the differences between the two depths were obvious to the subjects and the data were the same as on the surface, the 2 ATA dives were eliminated from the next series of dives in order to save diving time. In addition to the pre-dive and the data recorded at depth, VERs and EEGs were recorded during decompression at the 20 ft and the 10 ft stops. The standard decompression schedule in use for this series included breathing 100% oxygen at these two stops.

For the next group of eight men, run from Jan through Jun 1974, an additional experimental variable was added, the interval of time between dives. In addition, the depth was changed slightly to 189 ft (because of diving regulations), and the breathing of 100% oxygen was eliminated at the decompression stops at 20 and 10 ft.

Four of these men first made dives to 189 ft, followed by a second identical dive after 28 days. Three months later, they made two more dives to 189 ft separated by 3 days. The intention was to have the other four men make the four dives in reverse order, but chamber schedules precluded a fourth dive. Therefore, two of the men made three dives after intervals of 3 and of 28 days, and the other two men made the three dives in reverse order with intervals of 28 and 3 days. All eight men thus made dives that were separated from their last dive by both 3 and 28 days.

RESULTS

The results are organized into, first, the major findings for all subjects, for VERs and for EEG, and second, a number of minor comparisons. The latter are the differences between 2 and 7 ATA for the first eight subjects and between 3 and 28 day intervals for the second eight subjects.

The Evoked Response at 7 Atmospheres

Responses evoked by slow rates of stimulation - Sample evoked responses to flashes at a rate of one per second are shown in Fig. 1. Two of the curves are control curves: one, the pre-dive VER at the surface and the other, a post-dive run at the decompression stop at 10 ft. These are compared with the VER obtained at 7 ATA or about 200 ft. While all three curves are similar, one component - the activity at 160 msec - is much reduced at depth.

Figure 2 is an example for another subject who has a very different waveform. Again, the comparison of activity from surface to depth shows a large change around 160 msec; the reduction for this subject is evident for the entire time between 130 and 200 msec. This large change should be

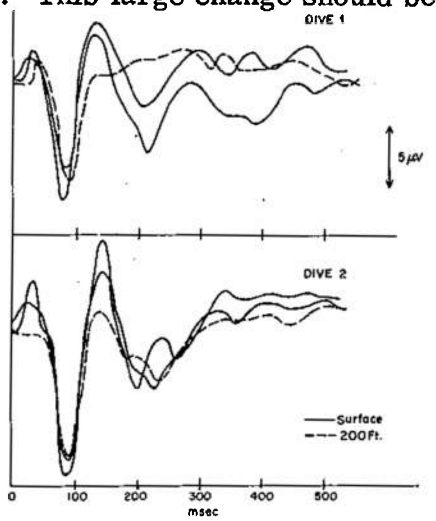

Fig. 1. Visual evoked responses for one subject showing the reduction at depth of the component around 160 msec in two separate dives

* *The VER to one flash per second was lost for one dive due to equipment malfunction. Therefore, the total number for this analysis is 15 rather than 16.*

contrasted with the general reproducibility of the VER under the same conditions; the two pre-dive VERs, as well as the two at 200 ft, are the same, despite the fact that they were recorded 28 days apart.

The latency and amplitude of the component around 160 msec was calculated for each of the VERs for all subjects.* The data, given in Table I, show the mean results for two dives for the same men, their first dive and one occurring at least one week later. The amplitude of the component at 160 msec is reduced at 7 ATA from its value at depth for both dives; the reduction is significant at the .001 level. There are no significant differences in latency.

The distribution of differences between surface and 7 ATA for each man was also determined and is summarized in the last column of Table I. These differences were normally distributed and ranged, for the first dive, from -.5 to 5.4 microvolts (μV) with a mean of 2.2 μV; only two of the 15 subjects had negative values. For the second dive, the range was zero to 7.0 μV with no negative values. There were no significant differences between the distributions for dive 1 and dive 2.

<u>Responses evoked by rapid rates of stimulation</u> - Typical VERs to flashes 16 times per second are shown in Fig. 3. For this subject, who followed the flash rate well, there are 16 individual responses in the one-second interval.

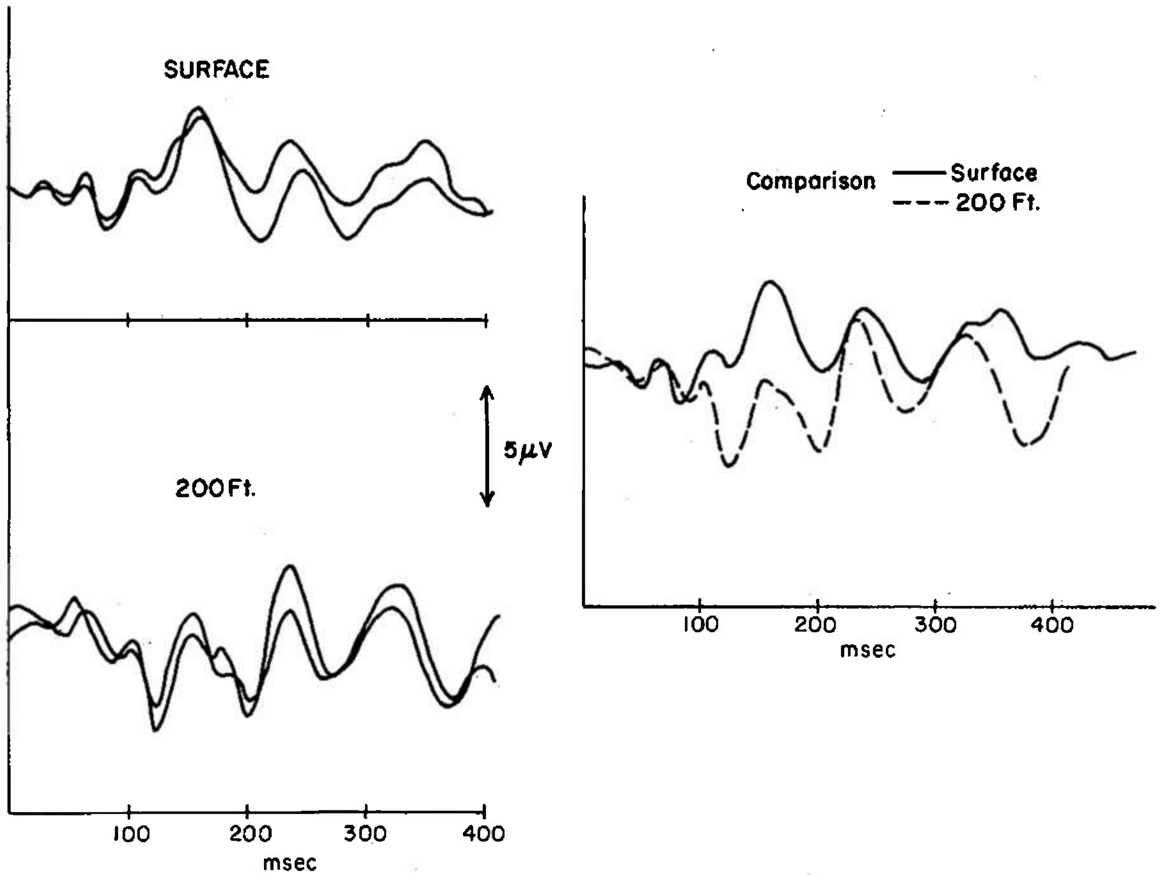

Fig. 2. Two VERs obtained at the surface (top left) and at 200 ft (bottom left) on dives 28 days apart. The comparison between the VER at surface and at depth is on the right.

The amplitude of each response is measured and a mean and standard deviation calculated. In addition, a Z score, or mean divided by the standard deviation, is obtained; this is a measure of the regularity of the VER which is independent of the amplitude of the response.

Decrements in both the amplitude and the regularity of the response are commonly found at 7 ATA. These vary from severe disruption of the response, illustrated in Fig. 4, to only moderate (Fig. 3) or none. Measures made on the 16 subjects are summarized in Table II. If the dive to pre-dive values were the same, the ratio would, of course, be 1.0. In fact, the amplitude measures for both dives are significantly less than 1.0; while the regularity ratios do not attain significance, the ratios for both dives are smaller than 1.0 and the ratio for the first dive is very close to the .05 level.

Table I. Comparison between the surface and 7 ATA for the amplitude and latency of a component around 160 msec. N = 15

	Amplitude in μVolts	Latency in msec	Distribution of differences Surface-Dive (μV)
		Dive 1	
Surface	3.9 ±4.7	159.9 ±8.4	+2.2# ±1.8
7 ATA	1.6 ±3.8	157.3±10.8	
t-test	4.77*	1.68	
		Dive 2	
Surface	3.8 ±4.2	160.2 ±3.8	+3.2# ±2.1
7 ATA	0.6 ±3.1	155.3 ±0.6	
t-test	5.88*	2.11	

* prob. < .001

\# sign. diff. from zero at p < .001

The range of individual differences in ratio varied from .336 to 1.155 for the dive/pre-dive amplitudes in dive 1 and from .70 to 1.32 for dive 2. Thirteen of the 16 men had ratios less than 1.0 for the first dive; for the second dive this number was reduced to 11 out of 16.

The regularity measures showed considerably more variability and ranged from .28 to 1.63 for dive 1 and from .18 to 1.73 for dive 2. Eleven of the 16 men had ratios of less than 1.0 on both the first and second dives.

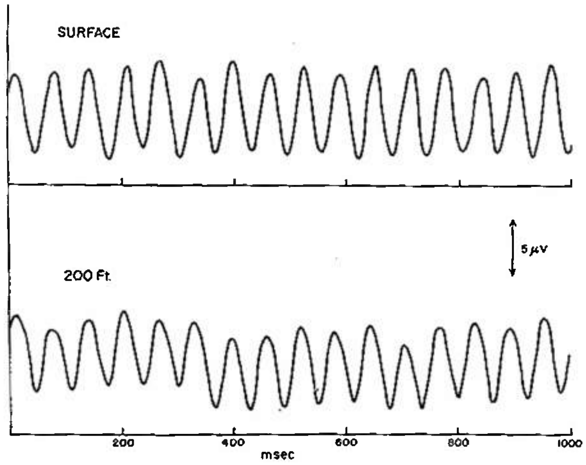

Fig. 3. *VERs to rapid flash rates for one diver determined at the surface (mean amplitude = 7.6 μv ±.58; Z = 13.1) and at depth (mean amplitude = 6.6 μv ±.62; Z = 10.6)*

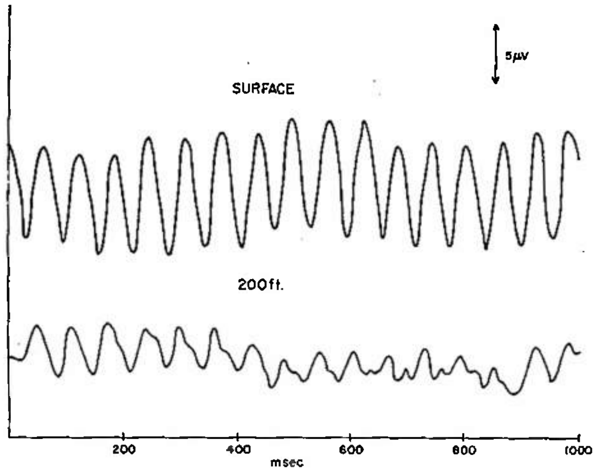

Fig. 4. *VERs to rapid flash rates for another diver at the surface (mean amplitude + 9.18 μv ±.70; Z = 13.11) and at depth (mean amplitude = 3.08 μv ±.84; Z = 3.67)*

Table II. Amplitude and regularity of VER 16s at 7 ATA
(Measures are the ratios of dive/pre-dive values.)
N = 16

	Dive 1	Dive 2
Amplitude	.80** ±.22	.89* ±.24
Regularity	.83 ±.40	.88 ±.41

* Significantly different from 1.0 at p <.05
** " " " 1.0 at p <.01

The Electroencephalograms at 7 Atmospheres

The raw EEGs from both the eyes-open and eyes-closed conditions were analyzed for the amplitude at each frequency in the range from zero to 50 Hertz, in 1/4-Hz steps. In addition, the EEGs recorded while the evoked responses were being measured were also analyzed. Table III contains typical results; data are given in ratios of dive to pre-dive amplitudes. For alpha, the mean amplitude ratios for the eyes-closed were slightly less than 1.0; on the first dive twelve of the sixteen men had ratios smaller than 1.0. However, there were large individual differences with the range varying from .34 to 2.2; the values thus are not significantly different from 1.0. On the second dive, eight of the men had ratios above 1.0 and eight below; the differences again are obviously not significantly different from 1.0.

Similarly, measures of alpha amplitude made with the eyes open and while observing the light flash, did not show differences from pre-dive to dive levels. Nor were there changes in the frequency of alpha during the dives; the mean frequency for 16 men was 10.2 ± .75 Hz at the surface, and 10.3 + .88 Hz during the first dive to seven atmospheres.

Table III. Measures of EEG made during dives. (Ratio of dive to pre-dive amplitudes)

	Amplitude of Alpha Eyes Closed		Amplitude at 16 Hz in VER 16	
	1st dive	2nd dive	1st dive	2nd dive
Mean	.88	.90	.70	.75
Standard deviation	.45	.31	.31	.23
t value	.99	1.22	3.67*	4.30*

* prob. <.001

Analysis of theta amplitude, during the eyes-open and eyes-closed conditions, likewise failed to show any significant differences at 7 ATA as compared to the surface.

On the other hand, the amplitude of the EEG at 16 Hz (Table III), measured with the diver looking at the light flashing at a rate of 16 times per second, is greatly reduced during the dive. For this measure, 14 of the 16 men had ratios smaller than 1.0 on the first dive and 13 men on the second dive. These differences are highly significant. In addition, the frequency analysis of the EEGs during VER 16 showed an additional peak at 32 Hz for some of the men. This harmonic peak, when it occurred in the pre-dive measures, was invariably reduced at depth, about as much as the peak at 16 Hz.

The Effect of Diving Experience on the VER and EEG Measures

The diving experience of these sixteen men varied considerably. A few of the men were qualified Navy divers with many years of diving history. Most, however, were chamber qualified only and, for many of them, these dives to 7 ATA were the first ever made to so great a depth. The men were therefore divided into two groups: four men with large amounts of in-water, Navy, diving experience were contrasted with the other twelve, whose diving was limited to chamber simulation.

The data on all the measures were averaged for the two groups and are summarized in Table IV. All the measures of the VER 16 - the amplitude, the regularity and the EEG response at 16 Hz - are clearly affected by diving experience. The dive to pre-dive ratios of the most experienced men approach unity (no decrement at depth) while those of the least experienced are, without exception, poorer. Further evidence of the effect of experience on these measures comes from the data of the repeated dives by the inexperienced men: all of their dive/pre-dive ratios improve

Table IV. The effect of amount of diving experience on the VER and EEG measures

	Most Experienced N = 4		Least Experienced N = 12	
	Dive 1	Dive 2	Dive 1	Dive 2
VER 1				
Loss of component in μvolts	2.32	4.90	2.22	2.57
VER 16				
Amplitude dive/predive ratio	.98	.95	.74	.86
Regularity dive/predive ratio	.87	.95	.81	.85
EEG				
Alpha amplitude	1.17	1.15	.79	.82
Amplitude at 16 Hz in VER 16	.92	.83	.63	.72

on the second exposure. Similar differences are found in the amount of alpha in the EEG.

On the other hand the loss of the component at 160 msec in the VER to a flash once a second does not appear to be related to experience; neither the comparison between the two groups nor the repeated exposure on dive two shows any indication of improvement. In fact, the second dive for both groups showed a larger decrement than the first dive.

Interrelations Between the Various VER/EEG Measures

Correlations have been computed for the various measures on the 16 men. These are summarized in Table V; the values used in the computations are the decrements, that is, the dive to pre-dive ratios or, in the case of the VER 1, the loss of component N 160. Correlations were calculated separately for the first and second dives and also for the average data for the two; the latter measure is presumably less subject to random variation.

Table V. Interrelations among VER and EEG decrements

Measures Correlated	Dive 1	Dive 2	Mean - both dives
Amplitude of alpha and VER 16	.01	-.11	.11
and EEG at 16 Hz	.40	.32	.36
and VER 1 loss of N 160	.29	.55*	.42
VER 16 and EEG at 16 Hz in VER 16	.50*	.32	.71**
Decrements in VER 16 and VER 1	-.341	.294	.16

* significant at <.05 level
** significant at <.01 level

The highest correlation shown, +.71 for the mean of both dives, is between the VER 16 amplitude and the amplitude at 16 Hertz measured in the raw EEG. This is reasonable of course since the two are different measures of essentially the same phenomenon. On the other hand, there is no correlation between the VER 16 amplitude and the loss in the VER 1 or the change in alpha amplitude. The other correlations, between alpha amplitude and the EEG at 16 Hz and the loss in VER 1, are low positive ones and generally not significant; they probably reflect little more than gross changes in amplitude of the overall EEG.

The Differences in Evoked Responses Measured at 2 and at 7 Atmospheres

A comparison of the amplitude of the evoked response to the rapid flash rates (VER 16s) at 2 and 7 atmospheres is shown in Fig. 5. These are the average data for the same eight men, during pre-dive measures, at depth, and during two post-dive sessions during decompression at 20 ft and at 10 ft. As part of the decompression schedule, the men had been breathing oxygen at both 20 ft and 10 ft prior to and during the VERs.

The amplitude of the VER 16s is significantly reduced beyond the pre-dive ($\underline{t}$ = 3.8, $\underline{p}$ <.01) at 200 ft but not at 33 ft. All scores during the decompression are elevated beyond the pre-dive level; it is possible that this is due to an effect of oxygen. The regularity of

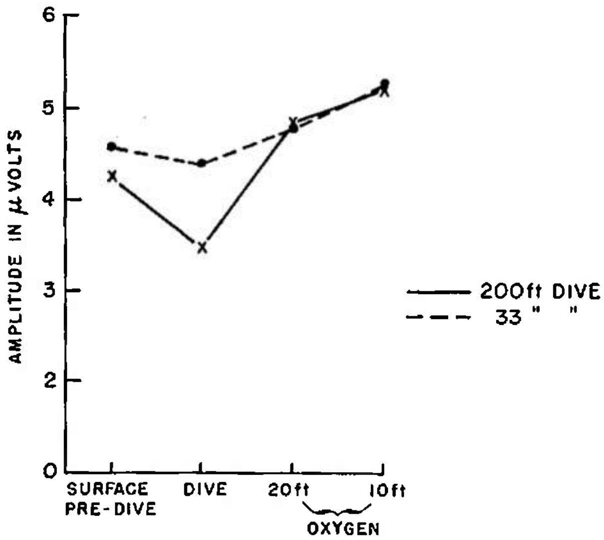

Fig. 5. A comparison of the average amplitude for 8 men of VERs to rapid flash rates obtained during dives to 200 ft and to 33 ft

the VER 16s for these same men was quite variable and there were no significant differences among any of the depths.

Comparison of Inter-Dive Intervals of 3 and 28 Days

Table VI is a comparison of the decrements in evoked responses for repeated dives made with varying time intervals in between them. Dive 1 refers to the first dive in at least three months. The column labelled three days later gives data collected on a dive which occurred exactly 3 days after another dive. The separation of one month is a dive 28 to 31 days following another dive with no dive in between. Seven men completed this program; one of the original eight was transferred in the middle of it.

Table VI. Comparison of decrements in the evoked responses with 3 and 28 day intervals between dives for seven divers. (Ratios Dive/Predive values)

	Dive 1	Dive 3 days later	Dive 1	Dive one month later
VER 16				
Amplitude	.68 ±.21	.80 ±.21	.76 ±.27	.91 ±.28
Regularity	.52 ±.19	.86 ±.47	.60 ±.34	.75 ±.34
VER 1				
Loss of component	3.8 μv ±2.1	4.2 μv ±3.5	3.0 μv ±1.1	4.9 μv ±1.2

There are large decrements in all average measures on almost all of the dives; the decrements shown in the dive 1 columns are all highly significant compared to the surface values. For the measures on the VER 16, there is evidence of improvement: each of the repeated dives show less decrement than dive 1. There is however no apparent effect of the inter-dive interval; there was as much improvement after a month as there was with only 3 days intervening.

For the VER 1, the decrements were all large and there was no evidence of improvement in any of the repeated dives. In fact, the amount of decrement on the repeated dives was even larger than in the first dive, although not significantly so. A similar analysis of the raw EEG data did not show any significant decrements on any of the dives, whether they were first or last in the series. This is in agreement with the data analysis of the EEGs of the total group of 16 men.

DISCUSSION

The major observations of this study are the decrements in the amplitude and regularity of the visual response evoked by rapid flash rates and the loss of a component at about 160 msec in the response evoked by a slow flash rate. These evoked response decrements can be contrasted with the lack of change manifest in the raw EEG under the same conditions. The data are thus in agreement with those from our previous dives; in fact, all of these effects have been reported previously.[4-7] However, these earlier dives have all employed very few subjects, usually two, and never more than four or five. Furthermore, it was often the case that one subject would respond as indicated above, while another would not. The major contribution of this investigation therefore is a quantification of the size of the individual differences for a large group of subjects.

The analysis of individual differences has revealed several important facts: First, a decrement in amplitude of the response to rapid flash rates occurs in the large majority of individuals on the first dive, a decrement which decreases in size with repeated dives. The amount of the decrement also decreases with real diving experience. Thus, if the population from which one is drawing subjects is one of first class Navy divers, as is generally the case with saturation dives, the chances of obtaining subjects who do not show a decrement are greatly increased. (The chances of obtaining subjects who do not become very narcotic also is presumably increased.) This accounts for inconsistent data in simulated saturation dives on two or three subjects.[6,7]

Similar statements can be made about the regularity of the response to rapid flash rates, although this decrement is, on the average, not as large or as reliable as the loss of amplitude in the response.

A second significant result comes from analysis of the individual differences in the response evoked by the slow flash rate. Here, too, the large majority of individuals show a decrement, the loss occurring in a component at about 160 to 170 msec after the flash of light. However, for this loss, there is no evidence of improvement, either on the second dive, or with general diving experience. This result is somewhat at variance with our previous finding of an improvement with repeated testing during a long saturation dive.[6] However, two points should be considered: first, the improvement came after 10 to 12 days of saturation with daily excursions to greater and lesser depths on air; and second, even after this extensive experience, the adaptation was not complete.

It therefore seems safe to conclude that the two decrements, in the responses evoked by rapid and by slow flash rates, have different underlying mechanisms.* One shows evidence of adaptation very quickly while the other does not and there is no correlation in the size of the losses among the sixteen

* *Indeed, the responses themselves probably have different underlying mechanisms. See for example, Regan's discussion[21] of the transient (VER 1) and the steady-state (VER 16) evoked responses.*

subjects. The underlying mechanism for these losses are not now known, although a search for them is the goal of other, ongoing research. The present evidence thus sheds little light on the question of why the size of the decrements in evoked responses is not predictable from the narcotic potency of narcotic gases.[13,14] It does however further emphasize the possible role of multiple sites and multiple mechanisms,[9] since we have evidence for two independent losses within the same modality while using the same measuring technique - the visual evoked response.

As far as routine EEG measurement is concerned, these results do not show any reliable changes in the EEG during bounce dives to 7 ATA. This does not mean that EEG changes will not occur under more severe environmental stresses; such changes are well-documented.[6,16-20,22,23] However, the evoked response is the most sensitive measure of brain functioning for these conditions.

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13. ABSTRACT

In order to assess individual differences in susceptibility to nitrogen narcosis, a group of 16 men made repeated air dives to approximately 200 ft in a pressure chamber. The visual evoked response of the men at depth revealed several decrements: in the response to a slow rate of stimulation, there was a highly significant reduction in a component around 160 msec; in the response to a rapid rate of stimulation, marked losses in amplitude and increases in variability were found. The latter changes were related to diving experience while the former were not. No significant changes were found in alpha or theta activity in the EEG.

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